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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/492,764	01/27/2000	Richard Jove	114205.1101	1344

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EXAMINER	
CANELLA, KAREN A	
ART UNIT	**PAPER NUMBER**
1643	

DATE MAILED: 02/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/492,764	JOVE ET AL.	
	Examiner	Art Unit	
	Karen A. Canella	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1,19,22,23,33 and 34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1,19,22,23,33 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/2/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 2, 21, and 24-27 have been canceled. Claims 1, 19, 22, 23, 33 and 34 have been amended and are under consideration.

2. Sections of Title 35, U.S. Code not found in this action can be found in a prior action.

3. Claims 1, 19, 22, 23, 33 and 34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

(A) As drawn to new matter

Claim 1 has been amended to specify the inhibition of the growth of cancer cells in a patient with antagonists having 3 to 12 amino acids comprising SEQ ID NO:20, 22, 24-28, 30-32 and 34-38. Claim 1 also recites the limitation "wherein said antagonist antagonizes STAT3 DNA binding and wherein said antagonist noncovalently binds to a STAT3 polypeptide". The claim then further specifies that the antagonist is a peptide "having" a length of 3 to 12 amino acids, comprising SEQ ID NO:20, 22, 24-28, 30-32 and 34-38. The specification identifies said peptides in Table 3 in an assay for the disruption of STAT3-DNA binding. The specification provides no evidence that said peptides "non-covalently bind to STAT3" as required by the claim. The specification identifies peptides that bind to full-length STAT3 in Table 1, and peptides which bind to the SH2 domain of STAT3 in Table 2. The instant peptides of Table 3 do not appear to be fragments of the peptides in Table 1 or 2 which have bee identified as having the ability to bind to STAT3. Thus, one of skill in the art would reasonable conclude that although the claimed peptide have been identifies as being able to disrupt STAT3-DNA binding, there is no objective basis for concluding that said peptides bind to STAT3 without further evidence that this is so.

(B)As drawn to inadequate written description

The instant method claims are reliant upon a genus of peptide antagonists to STAT3 which disrupt STAT3-DNA binding, wherein said genus includes peptides "having" a length of 3

to 12 amino acids, which comprise SEQ ID NO:20, 22, 24-28, 30-32 and 34-38. The term "having" is open language and equivalent to comprising. The peptides of SEQ ID NO:20, 22, 24-28, 30-32 and 34-38 are from 3, 4 and 6 amino acids in length. This does not provide adequate support for the limitation of having a length of 3 to 12 amino acids. The peptides which are identified in Table 1 and 2 include 12-mers and 7-mers, respectively. However, these peptides are not identified as having the ability to disrupt STAT3-DNA binding, nor are the claimed peptides fragments of said 12-mers or 7-mers. One of skill in the art would reasonable conclude that applicant was not in possession of the genus of peptides on which the instant method claims rely. Further, with regard to a peptide "having" an amino acid sequence of between 3 and 12 amino acids, it is concluded that the structural constraints imposed upon the identity of the antagonist peptides are minimal because the antagonists only need to minimally comprise between 3 and 12 amino acids and therefore encompass much larger polypeptide. The disclose of a very small peptide, such as a 3, 4 or 6-mer, does not provide adequate written description of the entire genus of peptides which include proteins which are much larger than the peptides and minimally comprise the very small amino acid sequences.

4. Claims 1, 19, 22, 23, 33 and 34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of

experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Claim 1 has been amended to specify the inhibition of the growth of cancer cells in a patient comprising administering antagonists having 3 to 12 amino acids comprising SEQ ID NO:20, 22, 24-28, 30-32 and 34-38. The specification states on page 64, that "the disruption of STAT3 DNA-binding activity with peptides containing as few as 3 or 4 amino acids, which is ideal for the synthesis of peptiomimetic combinatorial libraries". The specification states on page 6, lines 19-21 that "short peptides exhibiting these binding characteristics are identified as described herein, that are efficient inhibitors and potential lead compounds for future development of novel anti-cancer drugs". Thus, the specification is contemplating that the invention of disrupting STAT3-DNA binding by small peptides in vitro is only the beginning of a research effort to identify compounds which can be used as drugs. The specification does not teach drugs obtained thereby. The art teaches that the direct intracellular delivery of proteins or peptides is difficult due to the plasma membrane of he cell which prevents the uptake of macromolecules by limiting passive entry (Wadia and Dowdy, Advanced Drug Delivery Reviews, 2005, Vol. 57, pp. 579-596). The art teaches that this problem can be overcome by attachment of peptides and proteins to protein domains having cell membrane penetrating ability and identified the Drosophilae antennapedia protein as one such protein which was known in the art before the instant filing date (Wadia and Dowdy, ibid, page 581, first column, lines 26-31) . However, the instant claims require the antagonism of STAT3-DNA binding, which would occur in the nucleus, necessitating not only the penetration of the plasma membrane but the penetration of the nuclear membrane as well, as well as the migration of the peptide through the nuclear matrix to the area of the DNA where STAT3-DNA binding is occurring. There are no teachings in the art or in the specification for how to treat and individual having cancer in such a manner as the administered peptides would traverse the plasma membrane of tumor cells and traverse the nuclear envelope as well. The art teaches that the nuclear envelope differs in structure from that of the plasma membrane and that larger proteins are transported across the nuclear envelop by saturable pathways that are energy-and signal-dependent which include nuclear localization

sequences which (NLS) are commonly short stretches of amino acids rich in basic amino acid residues (Guo et al, WO 02/18572, page 3, lines 8-11). Thus, it appears as if the requirements for transversing the plasma membrane and penetrating the nuclear envelope are different as a result of the different structure of each. The specification provides no teachings as to the penetration of both the plasma membrane and the nuclear envelope of a tumor cell and the delivery of a quantity of the peptides of SEQ ID NO:20, 22, 24-28, 30-32 and 34-38 in such amounts as to be efficacious to a patient.

The art also teaches general problems with the administration of peptide and protein drugs, namely short half-life in vivo, necessitating multiple administrations (Johnson and Tracey, 'Peptide and Protein Drug Delivery', In: Encyclopedia of Controlled Drug Delivery, Vol. 2, 1999, pages 816-833). The art teaches that major stability, release and manufacturing challenges" (page 816, second column, lines 1-5) must be met in order to overcome the technical difficulties associated with the delivery of peptides in vivo. The specification does not teach a means for the delivery of these small peptides to the appropriate site and the efficacious uptake to result in the antagonism of STAT3-DNA binding and the inhibition of tumor-growth in a patient. Therefore it would be undue experimentation in order for one of skill in the art to determine the means by which the disclosed peptides could penetrate both the plasma membrane and the nuclear envelope in a manner which still maintains the ability of said peptides to antagonize STAT3-DNA binding, and then determine a means for the delivery of the peptides to the tumor in a patient in such quantities which would be efficacious to said patient, wherein said delivery means would include how to stabilize the peptides from degradation in vivo, or during the manufacturing process, and how to release the stabilized peptides in vivo in the appropriate quantities. Given the lack of teachings on all of the above, one of skill in the art would be subject to undue experimentation in order to make and use the instant invention.

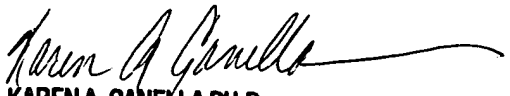
All other rejections and objections as set forth or maintained in the previous Office action are withdrawn in light of applicant's amendments.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 11 am to 10 pm, except Wed, Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Canella, Ph.D.
11/28/2005



KAREN A. CANELLA PH.D
PRIMARY EXAMINER